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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/625,963	07/26/00	STAUSS H	ICI 101

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EXAMINER	
DECLOUX, A	
ART UNIT	**PAPER NUMBER**
1644	10

DATE MAILED: 10/31/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/625,963	Strauss et al.
Examiner	**Art Unit**
D Cloux, Amy	1644

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 13, 2000*

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 4-20, and 22-38* is/are pending in the applica

4a) Of the above, claim(s) *8-14, 16-18, 20, and 22-38* is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 4-7, 15, and 19* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☒ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 9

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 1, 4-7, 15 and 19, in Paper No. 8 filed 8/13/01, is acknowledged. The traversal is on the ground(s) that the restriction requirement improperly divides the claims into groups of alleged inventions when in fact they should be divided into groups based on subject matter rather than sequence ID, and that the sequences should be part of a species requirement. This is not found persuasive because sequences constitute unique entities and are patentably distinct. The instant specification discloses on page 6 that the peptide comprising an amino acid sequence of SEQ ID NO:3 and the peptides comprising as amino acid sequence of SEQ ID Nos:1 and 2 are not even derived from the same polypeptide, SEQ ID NO:3 being a portion of the amino acid sequence of the human gata-1 protein, while SEQ ID NO:s 1 and 2 are each a portion of the amino acid sequence of the human WT-1 protein. The peptides comprising an amino acid sequence of SEQ ID Nos:1 and 2 have distinct non-overlapping sequences which confer distinct biochemical structure and properties, including distinct immunogenic epitopes.

The requirement is still deemed proper and is made final.

It is noted that the claims are being examined only to the extent of the elected invention.

2. Claims 8-14, 16-18, 20 and 22-38 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention. Election was made with traverse in Paper No. 8, mailed 7-23-01.

3. A) Formal drawings and/or photographs have been submitted which comply with 37 CFR 1.84.

B) The disclosure is objected to because of the following minor informality:

The use of the trademarks such as "QS21 Stimulon" and "Detox " page 24, lines 3 and 6, respectively, and so on, of the specification has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Each letter of the trademarks must be capitalized. *See MPEP 608.01(V)* and *Appendix 1.*

C) Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Great Britain on 11/2/1998. It is noted, however, that applicant has not filed a certified copy of the application as required by 35 U.S.C. 119(b).

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, In such full, clear, concise, and exact terms as to enable any person skilled In the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 4-6, 15 and 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 4-6, 15 and 19 recite a peptide comprising the amino acid sequence of SEQ ID NO:1, wherein the recited sequence is RMFPNAPYL, and a pharmaceutical composition thereof, and a vaccine comprising a peptide comprising the amino acid sequence of SEQ ID NO:1.

The instant disclosure of "a peptide comprising the amino acid sequence of SEQ ID NO:1" does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera. By reciting the term "comprising" in the instant claims, said peptide can also encompass an indeterminate number and type of additional amino acids, in addition to the amino acids recited in SEQ ID NO:1. With the exception of the peptide consisting of the amino acid sequence of SEQ ID NO:1, there is no description of the required structural and specific immunoprotective functional features of said peptides, or of the conserved regions that would be critical for these features. Further, the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the peptides encompassed, with the exception of a peptide consisting of the amino acid sequence of SEQ ID NO:1. Given the indefiniteness of the number and type of additional amino acids that may be encompassed by the peptide of the instant claims, the peptide, pharmaceutical composition thereof, and a vaccine comprising said peptide, the structure of "a peptide comprising the amino acid sequence of SEQ ID NO:1" is not conventional in the art and one of skill in the art would not recognize from the disclosure that applicant was in possession of the genus a peptide comprising the amino acid sequence of SEQ ID NO:1 encompassed by the claimed invention.

It is noted that though the claimed invention is directed to peptides and not cDNA, the principle of the following still holds for said peptides: a description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly&Co.*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Claims 1, 4-6, 15 and 19 recite a portion of a peptide comprising the amino acid sequence of SEQ ID NO:1, or a variant of a peptide comprising the amino acid sequence of SEQ ID NO:1. Given that a peptide comprising the amino acid sequence of SEQ ID NO:1 itself is not adequately described, (see previous two paragraphs) , it follows that a portion or a variant of said peptide is also not adequately described. Further, since applicants have not disclosed a variant or a portion of of a peptide comprising the amino acid sequence of SEQ ID NO:1, and given that the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify a peptide encompassed by said claims, the invention encompassing a portion of a peptide comprising the amino acid sequence of SEQ ID NO:1, or a variant of a peptide comprising the amino acid sequence of SEQ ID NO:1 is also not adequately described, along the lines of reasoning discussed supra. Despite knowledge in the art for producing variants, the specification fails to provide guidance regarding what deletions, additions, substitutions or alterations in SEQ ID NO:1 result in peptide variants that retain the ability to bind HLA-A2.

Claim 6 recites a peptide comprising the amino acid sequence of SEQ ID NO:1 wherein the peptide includes nonpeptide bonds. Given that a peptide comprising the amino acid sequence of SEQ ID NO:1 itself is not adequately described, (see previous two paragraphs) , it follows that said peptide having any number and type of nonpeptide bonds is also not adequately described. Further, since applicants have not disclosed a peptide comprising the amino acid sequence of SEQ ID NO:1 which includes non-peptide bonds, and given that the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify a peptide encompassed by said claims, the invention encompassing a peptide comprising the amino acid sequence of SEQ ID NO:1 which includes non-peptide bonds is also not adequately described, along the lines of reasoning discussed supra.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.)

6. Claims 1, 4-7, 15 and 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1, 4-7, 15 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for the recitation of a cancer vaccine for any cancer, including the certain types of cancer that over express WT-1. Neither does the instant specification provide enablement for how to make and use a peptide comprising SEQ ID NO:1, other than SEQ ID NO:1 itself, nor a portion of

a peptide comprising the amino acid sequence of SEQ ID NO:1, nor a variant of a peptide comprising the amino acid sequence of SEQ ID NO:1, nor a peptide comprising the amino acid sequence of SEQ ID NO:1 wherein the peptide includes nonpeptide bonds.

Furthermore, the specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed in the instant claims without an undue amount of experimentation. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of peptides broadly encompassed by the claims, nor with the large number of cancers.

The instant specification discloses cancers such as some leukemias that over express WT-1 (comprising SEQ ID NO:1), which the instant specification discloses as being derived from human WT-1 transcription factor. The instant specification also discloses on page 54 and in Figures 5 & 6, that the peptide consisting of SEQ ID NO:1 is I) presented by leukemic tumor cell lines that over express WT-1 and express HLA-A2, ii) that CTL directed to the peptide consisting of the amino acid sequence of SEQ ID NO:1 recognize CD34+ cells from HLA-A0201+ CML patients, as well as CD34+, HLA-A2+ leukemic tumor cell lines.

However, there is no reason to expect that said peptide would be effective as a cancer vaccine on any cancer cells not over expressing WT-1, or not expressing HLA-A2, because the antigen presenting structure would not be present, and/or the peptide antigen would not be present in sufficient quantity.

Janeway et al (Immunobiology 4th Edition, page 551) teaches that tumor peptide antigens can be targets of a tumor specific T cell response because they are not displayed on the surface of normal cells at least not at levels sufficient to be recognized by T cells, which is consistent with the decreased lysis by said CTL of CD34+ cells from HLA-A0201+ normal individuals as disclosed in Figure 6 of the instant specification.

Janeway et al also teaches that MHC Class I binding motifs of peptides is specific to each class I protein, and also that a peptide restricted by one MHC class I protein might not be immunogenic in an individual lacking said MHC class I protein (see page 121, page 569 and Figure 4.7 of Janeway et al. Immunobiology 4th Edition). Accordingly, there is insufficient guidance and direction from the instant specification that cancer cells which don't express HLA-A2 would be able to bind a peptide comprising or consisting of SEQ ID NO:1.

Therefore, it would require one of skill in the art undue experimentation to predict which cancers, other than those that over express WT-1 and that express HLA-A2, that would be effectively treated by a vaccine comprising a peptide comprising SEQ ID NO:1.

The instant specification provides insufficient guidance and direction that the recited peptide would be effective as a vaccine against any cancer, including those

that over express WT-1 and that express HLA-A2 .

The instant specification discloses in Figures 5 and 6 that a peptide of SEQ ID NO:1 is effective in killing cancer cells in vitro, but there is insufficient guidance from the instant disclosure on how to extrapolate from in vitro killing to in vivo killing.

Pages 53-54 disclose that the critical transformation events in CML and AML affect CD34+ cells, and that the in addition to the hallmark t(9;22) chromosomal translocation, the Wt-1 transcription factor is a candidate protein contributing to leukemogenesis, especially in view of its increased expression in CD34+ cells from CML and AML patients and in view of studies showing the in vitro enhancement of proliferation of hemopoietic cells with increased WT-1 expression, and that a recent study suggesting T cells specific for CD34+ progenitor cells are critically important in mediating anti-leukemic effects in CML patients.

However, Janeway teaches that melanoma tumor specific antigens which were recognized by CTL in vitro, were not expanded in vivo, suggesting that said peptides are not immunogenic in vivo (see page 551 of Janeway et al Immunobiology 4th Edition). Therefore, the in vitro data of the instant specification do not provide sufficient guidance and direction to extrapolate that a peptide comprising or consisting of SEQ ID NO:1 is immunogenic in vivo and would be effective as a cancer vaccine, absent evidence to the contrary.

In view of the insufficient guidance and direction from the instant specification and in the art, with regard to the efficacy of the recited peptide, including a peptide consisting of SEQ ID NO:1, as a cancer vaccine, it would require undue experimentation by one of skill in the art to develop a vaccine comprising a peptide comprising SEQ ID NO:1, that would be effective in treating any cancer, including cancers that over express WT-1, comprising the use of a peptide consisting of or comprising SEQ ID NO:1.

Further, the instant specification provides insufficient guidance and direction on how to make a peptide comprising SEQ ID NO:1, a pharmaceutical composition thereof, or a vaccine comprising a peptide comprising SEQ ID NO:1, other than SEQ ID NO:1 itself, nor a portion of a peptide comprising the amino acid sequence of SEQ ID NO:1, nor a variant of a peptide comprising the amino acid sequence of SEQ ID NO:1, nor a peptide comprising the amino acid sequence of SEQ ID NO:1 wherein the peptide includes nonpeptide bonds.

Class I molecules bind short peptides of 8-9 amino acids (see page 121 of Janeway et al). Therefore, the instant specification provides insufficient guidance and direction that a peptide larger than a peptide consisting of SEQ ID NO:1 would bind a class I molecule, as is encompassed by a peptide comprising SEQ ID NO:1 or a fragment thereof.

MHC restricted class I molecules bind a wide range of peptide antigens which would tolerate conserved substitutions, (see page 121 and Figure 4.7 of Immunobiology 4th Edition by Janeway et al. (1999)). However the instant specification provides insufficient guidance and direction that a peptide comprising non-

conserved substitutions within SEQ ID NO:1, especially at anchor residues, or any substitution outside of a peptide comprising SEQ ID NO:1, would still retain the ability to bind class I.

MHC restricted class I molecules form a pocket in which antigenic peptides fit and consequently bind (see Figure 4.3 and Figure 4.5 of Immunobiology 4th Edition by Janeway et al. (1999)). Therefore, the structure of a peptide must fit a class I molecule. The instant specification provides insufficient guidance and direction that a peptide comprising the amino acid sequence of SEQ ID NO:1 wherein the peptide includes any number and type of nonpeptide bonds will retain a structure that has the ability to fit into the MHC binding pocket.

Therefore, it would take undue experimentation by the skilled artisan to predict which of the recited peptides discussed supra (with the exception of a peptide consisting of SEQ ID NO:1) would bind MHC Class I.

In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention and this is not sanctioned by the statute.

7. The following is a quotation of the appropriate paragraphs of *35 U.S.C. § 102* that form the basis for the rejections under this section made in this Office action:

> a person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Semba et al (Gene 175: 167-172, 1996).

Semba et al teach a peptide from Xenopus laevis comprising SEQ ID NO:1. Therefore, the referenced teachings anticipate the claimed reference.

9. Claims 1 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Sharma et al (Cancer Res. 52:6407-64112, 1992).

Sharma et al teach a peptide from Rattus norvegicus comprising SEQ ID NO:1, see entire article, especially Figures 2-3. It is noted that intended use (such as use as a vaccine) does not carry patentable weight under art. Therefore, the referenced teachings anticipate the claimed reference.

10. Claims 1 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by

Buckler et al (Mol. Cell. Biol.. 11:1707-1712, 1991).

Buckler et al teach a peptide from Mus musculus comprising SEQ ID NO:1. It is noted that intended use (such as use as a vaccine) does not carry patentable weight under art. Therefore, the referenced teachings anticipate the claimed reference.

11. Claims 1 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Bluyssen et al (Eur. J. Biochem. 220:395-402, 1994).

Bluyssen et al teach a peptide from Cricetulus griseus which is a peptide that comprises a variant (RMSPNSPYV) of SEQ ID NO:1. It is noted that intended use (such as use as a vaccine) does not carry patentable weight under art. Therefore, the referenced teachings anticipate the claimed reference.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy DeCloux whose telephone number is (703) 306-5821. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 pm. a message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Amy DeCloux, Ph.D.
Patent Examiner,
October 26, 2001

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644